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CLINICAL RESEARCH

Thrombus in normal coronary arteries: Retrospective study and review of case reports

Thrombus sur coronaires normales : étude rétrospective et revue de cas cliniques

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KEYWORDS
Coronary thrombosis;
Prognosis;
Aetiology;
Myocardial infarction

Summary
Background. — Myocardial infarction is rarely caused by non-occlusive thrombus in angiographically normal coronary arteries. The cases reported in the literature are scarce and follow-up was usually short. The efficacy and tolerability of the exclusively medical treatment strategy used in most cases remain unknown.
Aims. — To evaluate efficacy of medical treatment and long-term prognosis in these patients.
Methods. — We retrospectively selected and analysed patients hospitalized in our centre between 1998 and 2008 for myocardial infarction caused by non-occlusive thrombus in angiographically normal coronary arteries (defined as stenosis < 30%), who were exclusively medically treated. A long-term follow-up was performed. A review of the literature regarding such cases was carried out.
Results. — Sixteen patients were identified; apart from smoking, they had few conventional cardiovascular risk factors. Two patients died in hospital. The 14 survivors were followed up for an average of 4.9 years and only one death (non-cardiac cause) and one stroke (related to supraventricular arrhythmia) occurred in this period. Medical treatment included the use of glycoprotein IIb/IIIa inhibitors in 75% of cases. The literature review revealed 36 similar cases due to multiple aetiologies—particularly coronary artery spasm and prothrombotic coagulopathies.
Conclusion. — Patients with myocardial infarction secondary to non-occlusive thrombus in angiographically normal coronary arteries seem to have a good long-term prognosis after the acute phase when treated with an exclusively medical strategy. However, initial clinical presentation was often severe, leading to early in-hospital death.

Abbreviations: TIMI, Thrombolysis in myocardial infarction.

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MOTS CLÉS
Thrombose coronaire ;
Pronostic ;
Étiologie ;
Infarctus du myocarde

Résumé
Contexte. — Les infarctus du myocarde peuvent, rarement, être causés par des thrombus non occlusifs sur des coronaires angiographiquement normales. Les cas rapportés dans la littérature ont été rares et leur suivi souvent court. L'efficacité et la tolérance du traitement médical exclusif, utilisé dans la plupart des cas, restent inconnues.
Objectif. — Évaluer l'efficacité du traitement médical et le pronostic à long terme chez ces patients.
Méthode. — Nous avons rétrospectivement sélectionné et analysé les patients hospitalisés dans notre centre, entre 1998 et 2008, pour un infarctus du myocarde causé par un thrombus non occlusif sur coronaires angiographiquement normales définies par des sténoses inférieures ou égales à 30 % et traités exclusivement médicalement. Un suivi à long terme a été effectué. Une revue de la littérature sur les cas similaires a été réalisée.
Résultats. — Seize patients ont été identifiés et hormis le tabagisme, ils avaient peu de facteurs de risques cardiovasculaires conventionnels. Deux patients sont décédés à l'hôpital. Les 14 survivants ont été suivis pendant 4,9 ans en moyenne, un décès de cause non cardiaque et un accident vasculaire cérébral relatif à un trouble du rythme supraventriculaire ont eu lieu. Le traitement médical comprenait l'utilisation des inhibiteurs des GPIIb/IIIa dans 75 % des cas. La revue de la littérature a révélé 36 cas similaires aux étiologies multiples, en particulier le spasme coronaire et les coagulopathies prothrombotiques.
Conclusion. — Les patients avec infarctus du myocarde secondaire à un thrombus non occlusif sur coronaires angiographiquement normales semblent avoir un excellent pronostic à long terme après la phase aiguë lorsqu'ils ont été traités exclusivement médicalement mais la présentation clinique initiale fut souvent sévère conduisant à des décès hospitaliers précoces.

Background

Acute coronary syndromes include several clinical and anatomical aspects of coronary disease, especially including intracoronary thrombus. Percutaneous revascularization of thrombus-containing lesions is associated with increased incidence of death and myocardial infarction [1]. However, intracoronary non-occlusive thrombi were rarely observed in patients without angiographic coronary lesions and have previously been proposed as a possible cause of myocardial infarction in those with normal coronary arteries [2]. The development of interventional cardiology allowed these thrombi to be identified in the acute phase of coronary syndromes. In the literature, case reports were scarce and follow-up was usually for less than 6 months. Exclusively medical treatment was used in most cases but its efficiency and tolerability remain unknown. Our study investigated the characteristics, aetiologies and long-term follow-up of patients with intracoronary non-occlusive thrombus without angiographic coronary lesions, who were medically treated in the acute phase. A review of the literature reporting such cases was performed.

Methods

Our study

Patients who were admitted to our institution with myocardial infarction with or without ST-segment elevation were screened retrospectively from January 1998 to October 2008. Coronary angiograms were reviewed by two independent experienced angiographers. Sixteen patients were identified who had intracoronary thrombus without significant coronary stenosis (angiographically defined as more than 30%) and received exclusively medical treatment during the acute phase. The angiographic presence of a thrombus was defined as a non-calcified filling defect outlined on at least three sides by contrast media. We included patients with thrombus greater or equal to grade 2 [3], thrombolysis in myocardial infarction (TIMI) flow 2 or 3 [4] and without significant coronary lesions (underlying or throughout the coronary tree; Fig. 1). Patients were excluded for the following reasons: if doubt remained about the underlying coronary lesion due to the thrombus being affixed to the artery wall; if they had an anatomical abnormality of the coronary arteries (dissection, ectasia); if they had thrombosis during the procedure; or if they required balloon angioplasty or stenting in the acute phase.

Age, sex, cardiovascular risk factors and left ventricular ejection fraction were recorded. Clinical conditions known to be associated with hypercoagulation, such as pregnancy, oral contraceptive or drug use, were searched for systematically. Coronary angiograms and treatments were detailed.

Follow-up was performed by telephone questioning of the patient's general practitioner and cardiologist in February 2009. In case of lack of information this could be completed by interviewing the patients. The following data were analysed: death (cardiac death or all-cause mortality), recurrence of myocardial infarction, need for revascularization, heart failure, ventricular arrhythmia, bleeding complication, stroke, thromboembolic event, left ventricular ejection fraction and medical treatment.

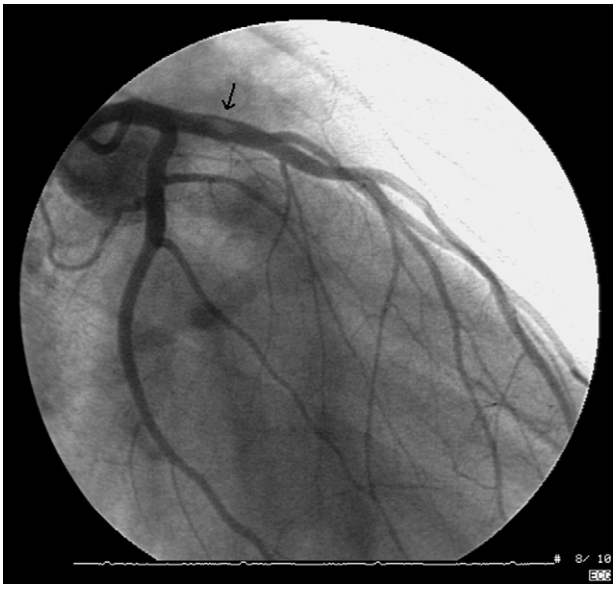

Figure 1. Coronary angiogram showing non-occlusive thrombus in the proximal left anterior descending artery without stenosis in one of our patients.

Review of the literature

We conducted a manual review of case reports using the PubMed database. Unrestricted database searches until January 2009 were performed using the Medical Subject Headings (MeSH) term ''coronary thrombosis''. Article references were reviewed in order not to miss other case reports. Some articles had several case reports, of which only one was selected.

We included case reports on patients with ST-segment or non-ST-segment elevation myocardial infarction, with angiographically confirmed thrombus greater or equal to grade 2, without proximal occlusion on the thrombus and with angiographically normal coronary arteries. Studies with insufficient information and those involving patients with angiographically atheromatous coronary lesions greater than 30%, anatomical abnormalities of the coronary arteries (dissection, ectasia), thrombosis during the procedure or post-mortem-visualized thrombus were excluded.

The following information was extracted from each study: first author; year of publication; journal; patient characteristics (sex, age, cardiovascular risk factors, Killip class); electrocardiogram; coagulation analyses; left ventricular ejection fraction; thrombus TIMI grade; localization; presence of distal embolizations; treatment; possible coronary angiography control; aetiology; and follow-up.

After a review of 1261 published articles, 196 were read in detail and 36 articles were finally selected (Fig. 2). Similar cases were published by Burzotta et al. [5] but were not included in this review because the patients were treated in our institution and were therefore included in our cohort.

Statistical analysis

All continuous variables are expressed as mean values ± standard deviations. Categorical variables are expressed as numbers of patients or percentages.

Table 1 Clinical and therapeutic characteristics of the patients in our cohort.

Characteristic	
Baseline characteristics at admission ($n = 16$)	
Men	11 (69)
Previous angina pectoris	0
Systemic hypertension	5 (31)
Diabetes mellitus	0
Hyperlipidaemia	2 (12.5)
Current smoker	9 (56)
Family history of coronary disease	3 (19)
Systolic blood pressure (mmHg)	121 ± 18
Diastolic blood pressure (mmHg)	76 ± 11
Pulse (beats per minute)	72 ± 12
Heart failure	4 (25)
Electrocardiogram	
ST-segment elevation	9 (56)
Non-ST-segment elevation	7 (44)
Cardiogenic shock	3 (19)
Pharmacological treatments in acute phase	
Thrombolytic agents (patients with ST-segment elevation)	2/9 (22)
Unfractionated heparin	13 (81)
Low-molecular-weight heparins	3 (19)
Aspirin	15 (94)
Aspirin + clopidogrel or ticlopidine	11 (69)
Glycoprotein IIb/IIIa inhibitors	12 (75)
In-hospital deaths	2 (12.5)
Pharmacological treatments at discharge ($n = 14$)	
Aspirin	14 (100)
Beta-blockers	14 (100)
Angiotensin-converting enzyme inhibitors	11 (79)
Statins	13 (93)
Low-molecular-weight heparins	10 (71)
Aspirin + clopidogrel or ticlopidine	12 (86)

Values are mean ± standard deviation or number of patients (%).

Table 2 Coronary angiogram characteristics in our cohort ($n = 16$).

Coronary angiogram characteristics	Number of patients (%)
Thrombus grade	
Grade 1	0
Grade 2	1 (6)
Grade 3	7 (44)
Grade 4	8 (50)
Location	
Left anterior descending coronary artery	7 (44)
Circumflex coronary artery	1 (6)
Right coronary artery	7 (44)
Left main coronary artery	1 (6)
TIMI grade flow	
TIMI 2	3 (19)
TIMI 3	13 (81)
Distal embolization	3 (19)
Multiple thrombi	1 (6)

TIMI: thrombolysis in myocardial infarction.

Table 3 Follow-up of our patients.

	Number of patients (%)
Clinical events ($n = 14$)	
Death	
All causes	1 (7)
Cardiac causes	0
Recurrence of myocardial infarction	0
Revascularization	0
Heart failure	0
Ventricular arrhythmias	0
Stroke	1 (7)
Thromboembolic events	0
Bleeding complications	0
Pharmacological treatments ($n = 12$)	
Aspirin or clopidogrel	11 (92)
Aspirin + clopidogrel	2 (17)
Beta-blockers	12 (100)
Angiotensin-converting enzyme inhibitors	7 (58)
Statins	12 (100)

Results

Our cohort included 11 men and five women, with a mean age of 48 ± 14 years. Mean body mass index was 26.4 ± 4.8 (half had a body mass index > 25). Mean left ventricular ejection fraction was 56.8 ± 14.2% (range 20—76%). None of the patients had previous angina and more than 50% presented with ST-segment elevation on electrocardiogram at admission. Patient demographics and clinical characteristics at admission are summarized in Table 1. The TIMI risk score [4] was less or equal to 3 for all patients and the mean Global Registry of Acute Coronary Events (GRACE) score [6] was 90 ± 27.

All patients received curative anticoagulation in the acute phase and 75% received glycoprotein IIb/IIIa inhibitors for at least 12 hours. Seventy-one percent of the survivors received low-molecular-weight heparins for at least 7 days. All patients received aspirin and 86% had both aspirin and clopidogrel or ticlopidine at discharge (Table 1).

Blood analysis showed severe renal insufficiency in one patient and slight renal insufficiency in four patients. Coagulation disorders were investigated in only three patients; the results were negative. One patient was treated for essential thrombocythaemia. Homocysteinaemia was analysed in half of our cohort; results were normal. Mean fibrinogen was 3.6 ± 1.5 g/L (range 2.1—6.8 g/L).

Retrospective analysis of coronary angiograms showed mostly high-grade thrombi (Table 2). Coronary angiogram control was done in nine patients. Of the four controls done on day one, three showed persistent thrombi. The thrombi had disappeared on all controls done after the third day of hospitalization.

Aetiologies were suspected in eight patients (Fig. 3). Among patients with a found aetiology, one patient aged 31 years had presented with a stroke 6 years earlier but died within the first 24 hours and it was not possible to obtain a complete coagulation analysis. No patient was human immunodeficiency virus positive. Among patients without a found aetiology, five had cardiovascular risk factors other than smoking and five were smokers versus three and four, respectively, among patients with a found aetiology.

Two patients died in hospital: the first after 24 hours due to refractory shock after left ventricular assistance for irreducible ventricular fibrillation and the second after 2 months due to septic shock. Mean follow-up was 4.9 years (range 6 months to 10 years) for the remaining 14 patients. One patient died 6 years later from a non-cardiac cause (septic shock in myeloproliferative syndrome secondary to thrombocytosis). One patient presented with a stroke in atrial fibrillation 3 years after myocardial infarction. All patients recovered a normal left ventricular ejection fraction (63.3 ± 5.7%). Events and treatment during follow-up are summarized in Table 3.

In our review of the literature (Table 4), the patients described were young (mean age: 36.3 ± 10.7 years). Eighteen were smokers but only five had another cardiovascular risk factor. Only one third of the patients had biological tests to search for coagulation disorders (10/36) or a previous known coagulation disorder (2/36). Distal embolization was observed in 20 cases. Coronary angiograms controls done within the first 72 hours after admission showed persistent thrombi in four cases and total disappearance in 10 cases. Only one patient died during hospitalization and no events were reported in patients monitored after hospitalization.

Table 4 Review of case reports with cardiovascular risk factors, coronary angiogram characteristics, treatment, aetiologies and follow-up.

Case reports	Sex	Age	CVRF	Smoker	Thrombus grade	Location	Treatment	Asp	Clop-Ticl	Hep	GP inh	Throm	OAT	Follow-up (months)	Aetiologies
Acar et al. (2008) [27]	M	55	No	No	4	RCA 1	Medical	Yes	Yes	Yes	Yes	No	No	6	-
Atmaca et al. (2007) [28]	M	54	No	No	4	LAD 1	Medical	Yes	No	Yes	Yes	Yes	Yes	0	Coronary embolism
Bashour TT et al. (1994) [29]	W	29	Yes	Yes	4	LAD 1	Medical	Yes	No	Yes	No	No	No	0	Coronary spasm
Bashour TT et al. (1990) [30]	M	35	No	Yes	4	LAD 1	Medical	Yes	No	Yes	No	No	Yes	0	Coronary spasm
Bauters et al. (2002) [31]	M	28	No	No	4	LAD 1	Medical	Yes	Yes	Yes	Yes	Yes	No	3	Myocardial bridging
Bickel et al. (2002) [32]	W	35	Nr	Nr	3	Bif LAD-LCX	Medical	Yes	Yes	Yes	Yes	No	Nr	0	-
Cay et al. (2006) [33]	M	39	Nr	Nr	4	RCA 3	Medical	Yes	Nr	Yes	Yes	No	Yes	0	Coronary embolism
Ciraulo et al. (1979) [34]	W	36	No	No	3	Marg 1	Medical	Nr	Nr	Nr	Nr	Nr	Nr	0	After pregnancy
Corre et al. (2002) [35]	M	25	No	No	Nr	LAD 1	Medical	Nr	Nr	Nr	Nr	Nr	Nr	0	Factor V Leiden mutation
Dagdelen et al. (2001) [36]	W	47	No	No	4	LAD 2	Medical	Yes	No	Yes	Yes	Yes	Yes	2	Coronary spasm
Doshi et al. (2003) [37]	M	38	No	Yes	3	LAD 1	Medical	Yes	No	Yes	Yes	No	No	0	Cocaine use
Eggebrecht et al. (2002) [18]	M	32	Yes	Yes	4	LAD 1	Medical + Thrombec	Nr	Nr	Yes	Yes	No	No	0	Sumatriptan
Feit et al. (1988) [38]	M	32	No	Yes	3	LAD 1 + RCA 1	Medical	Nr	Nr	Yes	No	Yes	Yes	24	-
Germing et al. (2006) [39]	W	37	No	Yes	4	Bif LAD-LCX	Medical	Yes	Yes	Yes	Yes	Yes	No	14	-
Guo et al. (2007) [40]	W	41	No	No	3	LAD 2	Medical	Yes	No	Yes	No	No	No	0	Myocardial bridging

Haude et al. (1998) [20]	M	43	Yes	Yes	3	LAD 1	Medical + Angiopl	Yes	Yes	Yes	Yes	Yes	No	6	-
Kaykcoglu et al. (2005) [41]	M	29	No	Yes	-	Bif LAD-Dg 1	Medical	Yes	Yes	-	No	Yes	No	9	Factor V Leiden mutation
Klein AJ et al. (2008) [22]	M	44	Nr	Nr	2	LAD 2	Medical	Yes	No	Yes	Yes	No	Yes	3	-
Klein KL et al. (1989) [42]	M	36	No	Yes	4	RCA 2	Medical	Nr	Nr	Yes	No	Yes	Yes	6	Paroxysmal nocturnal haemoglobinuria
Kosar et al. (2003) [43]	M	43	No	No	3	Bif LAD-Dg1	Medical	Yes	No	Yes	No	No	Yes	3	Coronary embolism
Kurisu et al. (2004) [24]	M	28	No	Yes	4	LAD 1	Medical	Yes	No	Yes	No	Yes	Yes	0	Myocardial bridging
Kutom et al. (1991) [44]	W	26	No	No	3	LAD 1	Medical	Yes	Nr	Nr	No	No	Yes	3	Lupus
Marcu et al. (2005) [21]	W	51	Yes	No	4	RVP	Medical + Angiopl	Yes	No	Yes	No	No	Yes	3	Coronary embolism
Ment et al. (2002) [25]	M	23	Yes	Yes	4	LAD 1, 2 & 3	Medical	Yes	No	Yes	Yes	No	No	0	Anabolic steroid use
Moriuchi et al. (1989) [45]	M	37	No	Yes	2	LAD 1	Medical	Nr	Yes	Nr	Nr	Yes	Nr	36	-
Nakagawa et al. (1994) [46]	W	54	No	No	3	LAD 2 + RCA 1	Medical	Nr	Nr	Nr	Nr	Yes	Nr	0	Progesterone + tamoxifen
Pamplona et al. (1997) [47]	M	35	No	Yes	4	LAD 3 + LCX 2 + RCA 2	Medical	Yes	No	Yes	No	Yes	No	0	Heavy alcohol ingestion
Parry et al. (1992) [48]	W	27	No	No	2	LAD 1	Medical	Yes	No	Yes	No	No	Yes	3	Still's disease + after pregnancy
Penny et al. (1985) [49]	W	17	No	Yes	4	LAD 3 + LCX 3	Medical	No	No	Nr	No	No	Yes	3	Factor XII deficiency
Rod et al. (1986) [50]	M	32	No	No	4	LAD 1	Medical	Nr	Nr	Yes	No	Yes	Nr	0	Cocaine use
Schlaifer et al. (2001) [51]	W	36	Nr	Nr	4	LMCA	Medical	Yes	No	Yes	Yes	No	Yes	24	Antiphospholipid antibodies syndrome

Table 4 (*Continued*)

Case reports	Sex	Age	CVRF	Smoker	Thrombus grade	Location	Treatment	Asp	Clop-Ticl	Hep	GP inh	Throm	OAT	Follow-up (months)	Aetiologies
Surder et al. (2006) [19]	M	26	No	Yes	4	LAD 1 & 2	Medical + Thrombec	Yes	Yes	Yes	Yes	Yes	No	0	Cannabis
Tatli et al. (2007) [52]	M	24	No	Yes	4	LAD 1	Medical	Nr	Nr	Nr	Nr	Yes	Nr	0	Cannabis
Unterberg et al. (1989) [53]	M	38	No	Yes	3	LMCA	Medical	No	No	Yes	No	No	No	0	After trauma
Van Langenhove et al. (2001) [23]	W	67	No	No	4	Bif LAD-LCX	Medical	Yes	No	Nr	Yes	No	No	4	-
Villota et al. (2004) [54]	M	26	No	Yes	4	LAD 1	Medical	Nr	Nr	Yes	No	Yes	Nr	6	Cocaine

Angiopl: balloon angioplasty; Asp: aspirin; Bif: bifurcation; Clop-Ticl: clopidogrel or ticlopidine; CVRF: cardiovascular risk factors (except smoking); Dg: diagonal artery; GP inh: glycoprotein IIb/IIIa inhibitors; Hep: heparin; LAD: left anterior descending coronary artery; LCX: left circumflex coronary artery; LMCA: left main coronary artery; Marg: marginal artery; Nr: not recorded; OAT: oral anticoagulant therapy; RCA: right coronary artery; RVP: retroventricular posterior branch; Throm: thrombolysis; Thrombec: thrombectomy.

Discussion

Our study showed that patients with myocardial infarction secondary to non-occlusive thrombus in angiographically normal coronary arteries had a good long-term prognosis after the acute phase but that initial clinical presentation was often severe, leading to early in-hospital death. This evolution was obtained with exclusively medical treatment in our cohort.

Our patients appeared somewhat different from patients included in acute coronary syndrome trials, as they were younger [2] and presented with few cardiovascular risk factors, apart from smoking. Cigarette smoking is known to promote atherosclerosis but also inflammation, coronary vasospasm and thrombosis, increasing platelet aggregability and fibrinogen levels, and altering fibrinolysis mechanisms [7]. Our cohort was clinically close to those described in myocardial infarction with normal coronary arteries [8]. Intracoronary thrombi were considered as a possible cause of myocardial infarction in patients with normal coronary arteries, with thrombus lysis before coronary angiogram explaining the absence of possible thrombus [2].

We have proposed an algorithm to summarize the different aetiologies found in our cohort and in the literature (Fig. 4). Coagulation disorders promoting thrombosis, such as thrombocytosis in one of our patients, were a major cause. Thrombophilia, including antiphospholipid antibodies syndrome, was traditionally associated with venous thrombosis but must be sought in young patients presenting with coronary thrombosis without atherosclerotic signs [9,10]. Previous studies of patients with myocardial infarction with normal coronary arteries reported an increased prevalence of genetic prothrombotic factors or coagulation abnormalities [8,11] that were underestimated in our cohort and probably in the literature because some of the published cases were old and because the frequency of complete coagulation assessments was low. Coronary vasospasm might promote thrombi by reducing the lumen diameter and also blood flow; it can be provoked by several substances, such as cocaine, cigarettes, cannabis and alcohol. However, no provocation test was done in our cohort. Massive alcohol intake was proposed as a possible cause in two patients in our cohort, as this can promote thrombi due to intense vasospasm [12]. Inflammation during severe sepsis was another aetiology; during severe sepsis, endotoxins stimulate the expression of genes encoding procoagulant molecules and the endothelial cell production of the fibrinolytic inhibitor plasminogen activator inhibitor-1 [13]. Hormonal changes with oestroprogestative therapy or pregnancy have been shown to be associated with an increased risk of arterial thrombosis [14]. We found one case of anaemia related to vitamin B12 deficiency in our cohort. Vitamin B12 was negatively correlated with total homocysteine, a known thrombosis risk factor due to its actions on coagulation and endothelial function [15]; its role in our patient was hypothetical. Finally, we must underline that atherosclerosis might represent a cause in some patients. In our cohort, patients without a found aetiology had more cardiovascular risk factors. The coronary arteries were defined as normal using coronary angiography and it is possible that plaque rupture or endothelial erosion causing thrombus may have been missed on the coronary angiogram.

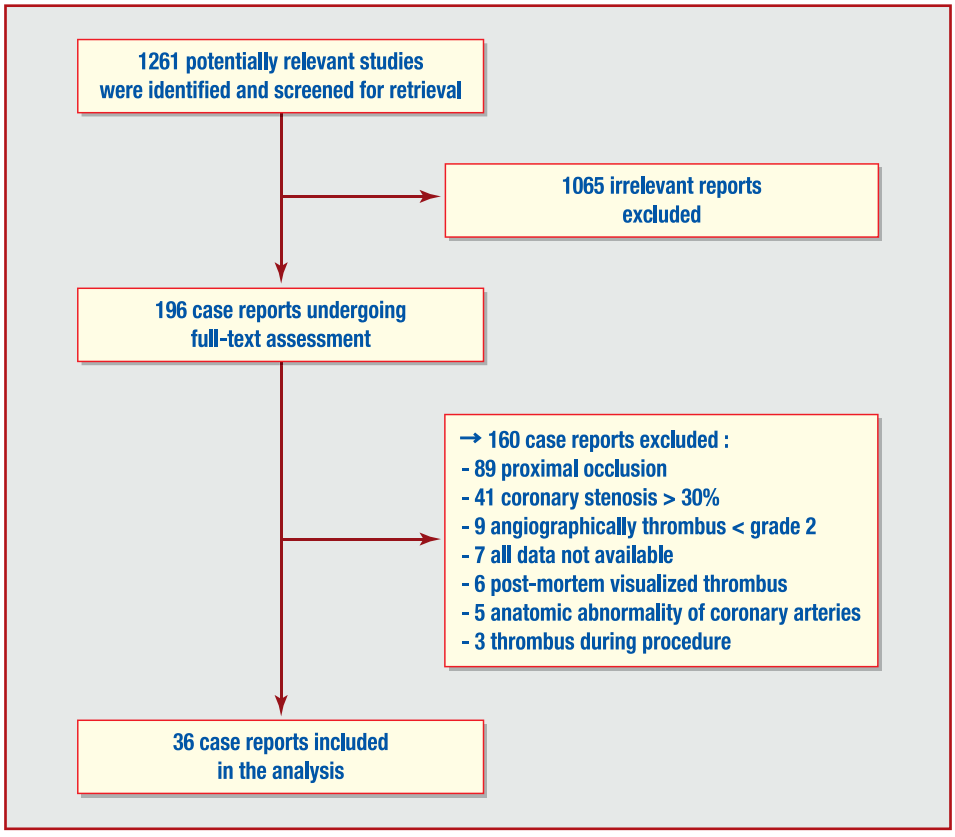

Figure 2. Flow diagram for case report selection.

Our study showed good long-term prognosis in hospital survivors. We found a global survival of 93% after hospitalization with a mean follow-up of 5 years, which was close to survival described for patients who had an acute myocardial infarction with angiographically normal coronary arteries (between 95.5% at 3 years [8] and 100% at 10 years according to the studies [16]). In contrast, studies of myocardial infarction irrespective of the importance of coronary lesions showed a dramatically worse long-term prognosis [6]. However, in the acute phase, more than half of our patients presented with ST-segment elevation myocardial infarction and cardiogenic shock was present in two of our patients. The absence of preconditioning in our patients, who were young and had no previous angina, could explain hospital mortality [17]. Long-term, one of our patients died from myeloproliferative syndrome secondary to thrombocytosis, showing the importance of the aetiologies in this syndrome. However, survival without cardiac events after hospitalization was 100% for our patients. In the literature, no events have been reported in the follow-up of patients, at least at mid-term.

All of our patients were medically treated in the acute phase. Other therapeutic strategies, including thrombectomy in two cases [18,19] and balloon angioplasty in two other cases [20,21], were rarely used in the same kind of patient, but were successful. Despite aggressive

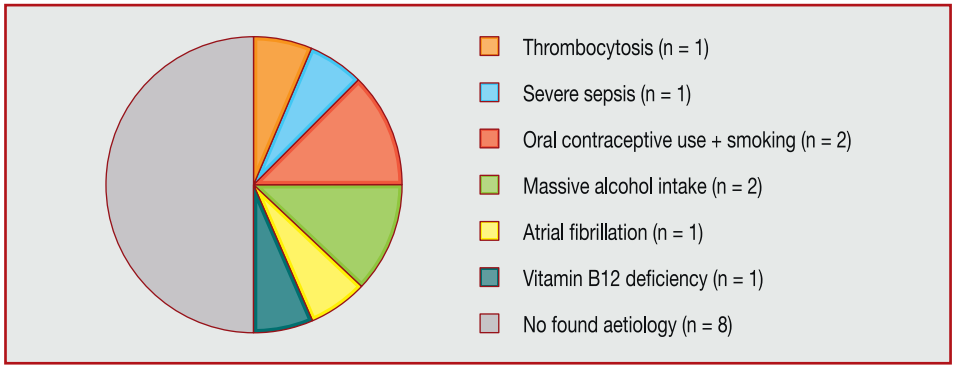

Figure 3. Distribution of suspected aetiologies in our cohort.

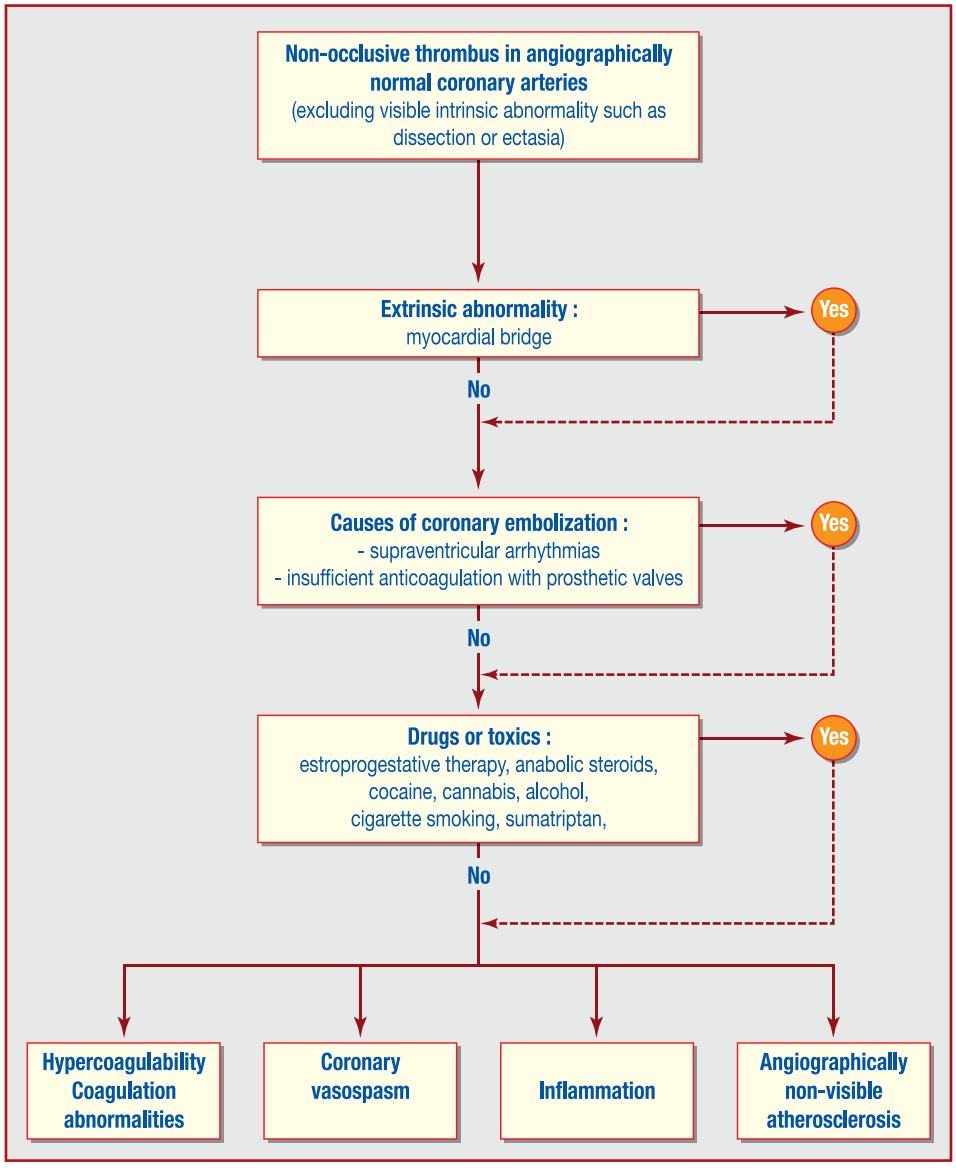

Figure 4. Proposed algorithm of aetiologies of thrombus in angiographically normal coronary arteries. It should be noted that intracoronary thrombus in the same patient could have multiple aetiologies.

anticoagulant and antiaggregant treatment, we observed no haemorrhagic complications in our cohort; their young age and few haemorrhagic risk factors justified aggressive medical treatment. Glycoprotein IIb/IIIa inhibitors were widely used in our study and probably brought an additional benefit, promoting thrombus lysis [3].

A coronary angiogram control was done in most cases. This control aimed to ensure the absence of underlying coronary lesions, which can be hidden by thrombi in the acute phase. Intravascular ultrasound analysis was not done, unfortunately, but can be recommended in these patients to gain a better understanding of pathophysiology and to avoid missing inconspicuous atherosclerosis. Thrombus persistence was not correlated with later evolution in our study. Frequency of persistent thrombi during the first 48 hours associated with embolic risk during the procedure should represent an incentive to extend these controls beyond 72 hours in the absence of clinical instability.

Study limitations

We studied a specific population of patients with intracoronary thrombus in angiographically normal coronary arteries or without significant lesions (> 30%), excluding occlusive thrombi. Poor visualization of the distal coronary artery and potential underlying lesions justifies the decision to exclude occlusive thrombi. Moreover, in the acute phase of myocardial infarction, the coronary artery must be reopened and angioplasty will be mandatory in most cases.

One of the main limitations was the small size of our cohort. However, as evidenced by review of the literature, our cohort is the largest reported to date with this specific clinical entity.

In our study, the coronary arteries were defined as normal using coronary angiography, which may misidentify atherosclerotic plaques with outward growth. No patients had angiographic evidence of plaque rupture. Systematic

intravascular ultrasound analysis was impossible due to the retrospective nature of this study; it was carried out in six patients in the literature, showing an absence of atherosclerosis in two cases [22,23] and inconspicuous signs of atherosclerosis in the other cases [18,20,24,25]. Physiopathological mechanisms causing these thrombi may be different from classical plaque rupture. Endothelial dysfunction, the importance of which has been emphasized in patients with or without coronary lesions [26], may play a leading role.

Conclusion

In our study and in the literature, patients with myocardial infarction secondary to non-occlusive thrombus in angiographically normal coronary arteries seem to have a good long-term prognosis after the acute phase, but clinical presentation was often severe leading to early in-hospital death. Our conclusions should be tempered by the small number of patients described. Exclusively medical treatment in our patients showed excellent long-term tolerability and efficiency. Many aetiologies, most of which are curable, should be searched for, with detailed examination and coagulation tests. There were numerous pathophysiological underlying mechanisms, probably associated with and similar to those described for myocardial infarction with normal coronary arteries, of which our cohort was probably a subgroup.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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